

REMARKS

Claims 116-133 were previously pending in this application. Claims 116-119, 121-125 and 132 have been amended to clarify the claim language. Support for the amendments can be found in the specification, at least at page 4, lines 25-29. As a result, claims 116-133 are pending for examination with claims 116 being an independent claim. No new matter has been added.

Rejections Under 35 U.S.C. § 103

The Examiner rejected claims 116-133 under 35 U.S.C. § 103(a) as being unpatentable over Gottlieb et al (Genetics 137: 107-120, 1994) in view of Martinelli et al. (Semin. Cell Dev Biol. (5):459-67, 1997). Applicant respectfully traverses the rejection.

The Combination of Gottlieb and Martinelli References Does Not Provide All Elements of the Claimed Invention

1. The Gottlieb Reference Lacks Several Elements of the Claimed Invention

The Examiner states that Gottlieb teaches a “method of making *C. elegans* libraries based upon phenotypic profiles of the worm (abstract).”(emphasis added) The Examiner also stated that Gottlieb teaches “subsequent screening of phenotypic profiles of worms each of which has different defects.” Regarding the compound of Applicant’s claims, the Examiner stated that Gottlieb teaches “screening of *C. elegans* libraries by exposing the variety of mutant worms to a chemical compound e.g., SDS.”(emphasis in original)

Applicant’s claimed invention is a method of determining the effect of compounds (e.g., chemicals) on the phenotype of nematodes. In particular, pending claim 116 recites a method for testing the influence of a compound on a *C. elegans* nematode. Unlike Gottlieb’s disclosure (as characterized by the Examiner), Applicant’s claim does not recite making *C. elegans* libraries or screening the phenotypic profiles of worms having pre-existing defects, i.e., the phenotype that results from a genetic defect or mutation. Instead, Applicant’s claimed invention is to expose a nematode to a compound, determine the resulting phenotype of the nematode exposed to the compound (the “phenotypic profile”), and then compare the phenotypic profile so determined to a reference library of phenotypic profiles.

Gottlieb looked at the influence of three genes, *daf-2*, *daf-16*, and *daf-23* on dauer formation. To determine the effects of these genes, Gottlieb constructed a series of *C. elegans* mutants having various combinations of mutant alleles of these genes. As a part of testing the mutant worms, Gottlieb used a standard assay of dauer formation, the ability of the worms to survive SDS exposure. See p. 109, left column, “Dauer formation in liquid” (“dauer formation was measured as the percentage of animals that survived a 30-min incubation in 1% SDS.”) and “Dauer formation on plates in *daf-16*; *daf-2* experiments” (“Dauer formation was measured as the percentage of animals that survived.”). See also p. 114, left column: “The efficiency of dauer formation in pheromone was monitored by determining the percentage of animals which acquire resistance to SDS.” See also figure legend for Fig. 3. Thus, SDS exposure was a means of determining the amount of dauer formation, not for determining the effect of SDS on *C. elegans* phenotype, because the *C. elegans* phenotype was determined by the genotype of the *C. elegans*.

Therefore, Gottlieb does not provide for testing the influence of a compound as in Applicant’s claimed invention.

Moreover, Gottlieb does not provide another element of Applicant’s claimed invention: “measuring a plurality of changed characteristics in the nematode upon exposure to said compound”. Gottlieb determined the effect of three *daf* genes on dauer formation after pheromone treatment (see p. 109, left column, “Dauer formation in liquid”). Gottlieb did not look at changed characteristics that result from exposure to SDS, because dauers were already formed by pheromone treatment of the mutant worms.

Further, Gottlieb measured a single phenotypic characteristic: dauer formation. In contrast, Applicant’s claimed invention recites that a plurality of characteristics is measured. A plurality is more than one.

Therefore, Gottlieb does not provide for measuring a plurality of changed characteristics as in Applicant’s claimed invention.

Accordingly, Gottlieb fails to teach or suggest several of the elements of Applicant’s claimed invention.

2. The Martinelli Reference Does Not Provide the Elements Missing from Gottlieb

The Examiner acknowledged that Gottlieb does not teach another element of the claimed invention: “comparing the generated phenotypic profiles with reference phenotypic profiles stored electronically on a database.”

The Examiner stated that Martinelli teaches a gene expression and development database (ACeDB) for *C. elegans* in which gene expression data are linked to genes, sequences, cells, organs and the developmental stage in which expression occurs. The Examiner also stated that Martinelli further teaches that “such an approach can be used to compare phenotypic profiles.” The Examiner suggests that the reference to the “Angler” accessory program in the abstract of Martinelli discloses or suggests the element of Applicant’s claimed invention relating to comparing the phenotypic profile to a library of reference phenotypic profiles stored electronically on a database.

Applicant respectfully disagrees. A close reading of Martinelli indicates that the Angler program is used to obtain more information about the cells in a Nomarski image. Martinelli suggests complementing the ACeDB with the Angler program to view particular cells and cell lineage. It is clear from the description of the Angler program (see page 466) that Angler is an image database of cells and cell lineages. The Angler database includes images of cells and lineages of wild-type worms, more particularly of wild type embryos, and even more particularly pictures of embryos taken at various time points until 230 min. Martinelli et al does not indicate that the Angler program provides a phenotype database describing and documenting phenotypes. To the contrary, Martinelli indicates at page 466, first column, 4th paragraph, that the Angler program is used to search on cells. It is not mentioned in Martinelli that Angler can be used to search for (i.e. ,to compare) phenotypes.

This is not the same action as (or even similar to) Applicant’s invention in which the phenotypic profile generated following exposure to a compound is compared to a library of reference phenotypic profiles. Thus, in Applicant’s invention, a set of phenotypic characteristics (e.g., characteristics A, B, C, D, ..., N) is compared to a library of phenotypic profiles of these characteristics. In contrast, Martinelli provides for obtaining cell lineage data and schematic views of cell positions that corresponds to Nomarski image data. Thus the Angler program referenced by Martinelli is providing additional data about the same characteristics, but does not

provide for comparing a set of phenotypic characteristics against a library of reference phenotypic profiles as in the claimed invention. Therefore, it is submitted that based on the teaching of the Martinelli reference, neither the ACeDB nor the Angler can be used to compare phenotypes, and that therefore this reference misses an important element of the invention.

Moreover, Martinelli does not provide the other elements of the claimed invention that are lacking from the Gottlieb reference, as noted above.

Accordingly, the combination of Gottlieb and Martinelli references fails to provide all of the elements of Applicant's claimed invention, and therefore the combination of these references is insufficient to render the claims obvious.

There is No Motivation to Combine the Gottlieb and Martinelli References

Applicant asserts that no suitable motivation exists to combine the Gottlieb and Martinelli References to make a *prima facie* case of obviousness.

Gottlieb teaches that certain *daf* mutants influence dauer formation as induced by pheromone treatment. The only phenotypic characteristic measured or observed by Gottlieb was dauer formation.

Martinelli teaches a database for storing and disseminating data on *C. elegans*. The database stores and links data on gene expression patterns to genes, sequences, cells, organs and the developmental stage in which expression occurs (see Abstract).

Gottlieb does not suggest comparing its data on *daf* mutants and dauer formation to other phenotypes through the use of a database. Martinelli likewise does not suggest that its database can be used for comparative purposes, rather its purpose is to "store and disseminate most types of *C. elegans* data, and ... for genome sequencing projects." See Abstract. Most particularly, Martinelli does not teach or suggest the use of the database to compare a phenotypic profile against stored phenotypic profiles.

Thus, neither Gottlieb nor Martinelli provide the requisite motivation to combine their teachings, which as noted above, would not in any case provide all of the elements of the

claimed invention. Without a proper motivation to combine these references, the obviousness rejection must fall.

The Examiner's suggested motivation to combine these two references is that "electronic data bases provides easy access to the stored information." The mere existence of the database as provided in Martinelli is insufficient to provide motivation, however, because a database by itself does not provide any motivation to carry out the step of comparing phenotypic profiles as claimed by Applicant.

The Examiner states that one skilled in the art at the time of filing would modify the method of Gottlieb, who teaches a method for screening compounds and *C. elegans* libraries based upon phenotypic profiles by incorporating the phenotypic information into an electronic database as taught by Martinelli, and the person of skill in the art would do so because electronic database provide easy access to the stored information.

Applicant also respectfully disagrees with this argument because as mentioned above: Gottlieb does not provide a method for screening compounds, and Martinelli does not teach incorporation of phenotypic data in a database. Thus, there is not suitable motivation to combine the references, at least because neither Gottlieb nor Martinelli teach or suggest the comparison step specifically claimed by Applicant.

Accordingly, because the combination of Gottlieb and Martinelli lacks elements of the claimed invention and because there is not proper motivation to combine these references, withdrawal of the rejection under 35 U.S.C. 103(a) is respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 117-118 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner indicated that it is unclear what is the criterion that defines "the strict standard protocol of measurement."

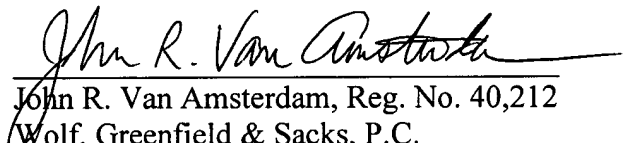
Applicant has amended claims 117 and 118 to clarify the claims. Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
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